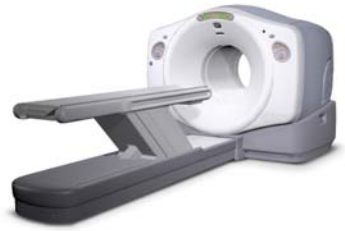
GE Healthcare

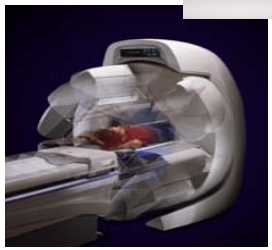
The development of imaging agents for diagnosis and therapy monitoring

Jonathan Allis
Global Head of Imaging
Medical Diagnostics

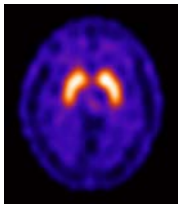
imagination at work

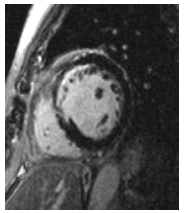
GE Healthcare

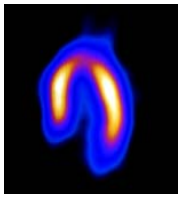


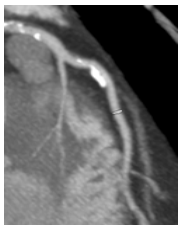




Imaging, Monitoring, IT

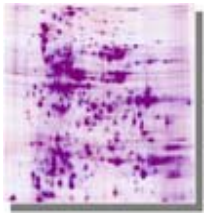









Medical Diagnostics


Life Sciences

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* Some products shown not available in the USA

Medical Diagnostics R&D

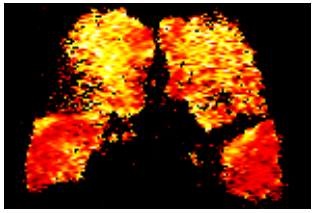
Next generation X-ray and MR contrast

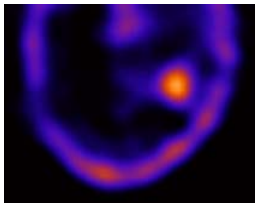
Polarized gases for Respiratory disease

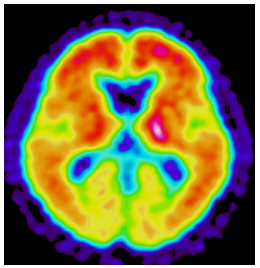
Molecular agents for Angiogenesis, Alzheimer's, Parkinson's, Heart failure, Bladder and Prostate Cancer (SPECT, PET, Optical, MR, Ultrasound, CT)

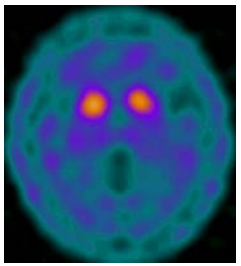
Our diagnostics are developed like any other pharmaceutical

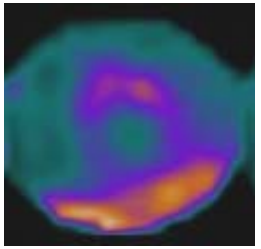
Same issues regarding variation and recruitment, complicated by multi centre imaging and combination product nature

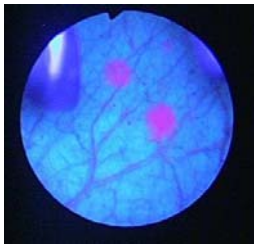












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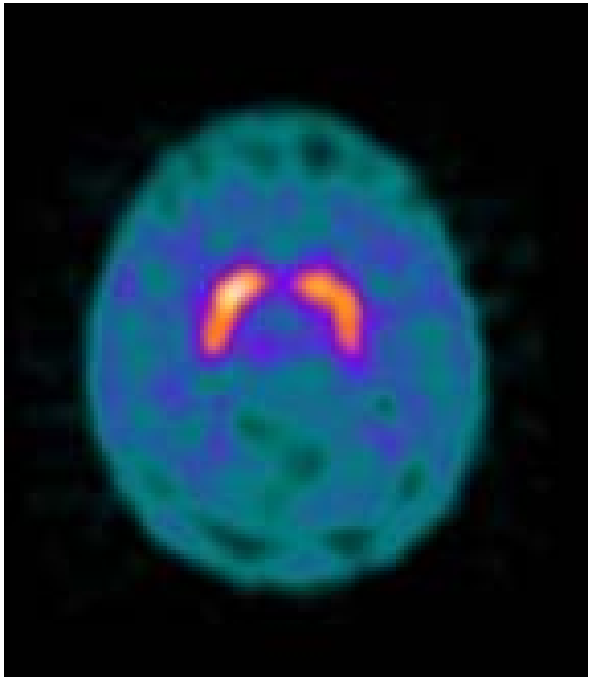
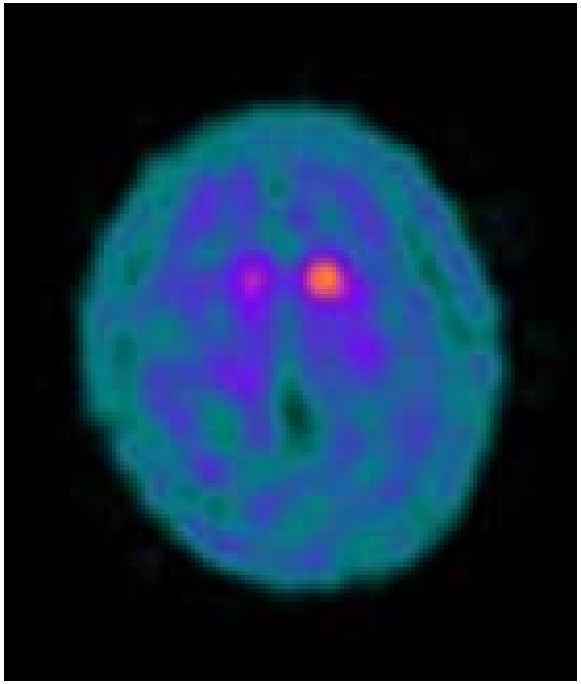
* None of the agents shown available in the USA

DaT transporter SPECT imaging



High uptake
Healthy



Low uptake
Parkinson’s

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The Statistical Challenge

Calculate N, the minimum number of subjects in the trial

Power of study

Variance in study

$$N > \frac{(u+v)^2(\sigma_1^2+\sigma_0^2)}{(\mu_1-\mu_0)^2}$$

Improve imaging process
- Build in Quality
- Reduce number of Trial Centres
- Analysis Software

In the trial, all you can control is the variance in imaging (drug substance, scanner, user, post-processing and analysis)

Receptor- Ligand biology and chemistry

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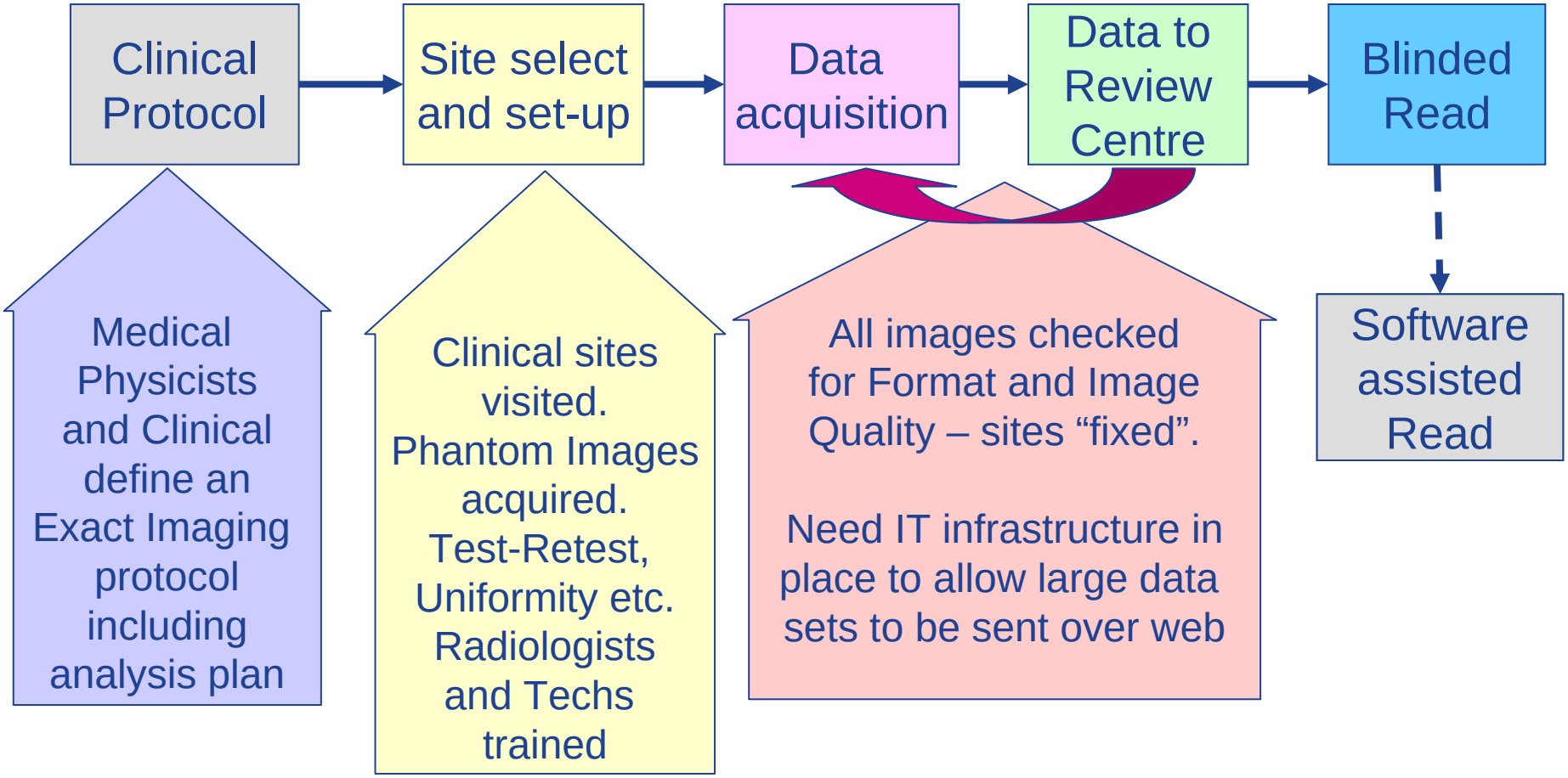
The Clinical Trial Process and Quality



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Advice from Regulatory Agencies

FDA's Critical Path Initiative to Transform Drug Development

Central focus is on development of biomarkers, imaging and other evaluative technology.

Imaging techniques must be standardized across multi-centre trials and for imaging systems from multiple vendors

Implement the same imaging protocols at all clinical sites

Conduct on-site training, monitor sites and react to non-compliance quickly

Avoid manual image processing techniques as much as possible, select and develop semi automated/automated methods

Some examples from MR trials

Study	Accuracy X-ray = Gold
GE Omniscan pilot MRA study	75%-78% (NE ~16%)
Non-GE MRA study (2 “approvable” letters)	73%-79%
GE Omniscan MRA Recent study	85%-89% (NE < 5%)
GE Omniscan Cardiac Perfusion	NE~30%+

No Image QC function

Image QC for all of study

Bleeding Edge

With quality process in place, non-evaluable rate falls, and data quality improves. Some studies are just very hard to do.

Medical Diagnostics Imaging Network

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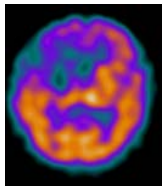
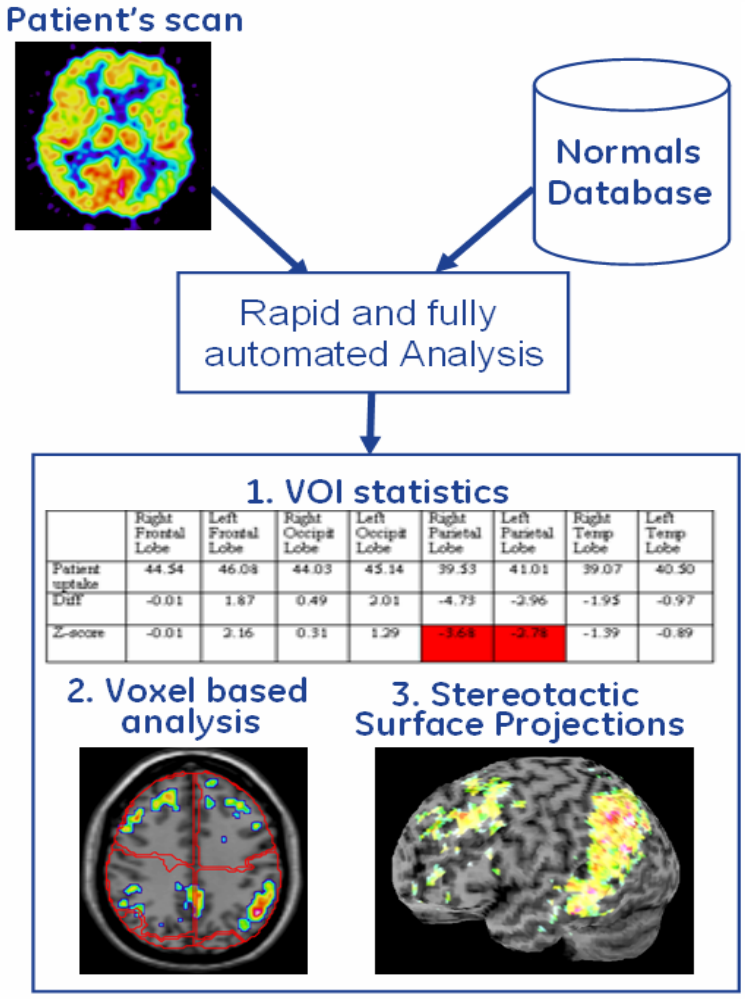
From Images to Information

Traditional “Imaging”



Future model



	Right Frontal Lobe	Left Frontal Lobe	Right Occipit Lobe	Left Occipit Lobe	Right Parietal Lobe	Left Parietal Lobe	Right Temp Lobe	Left Temp Lobe
Patient uptake	44.54	46.08	44.03	45.14	39.53	41.01	39.07	40.50
Diff	-0.01	1.87	0.49	2.01	-4.73	-2.96	-1.95	-0.97
Z-score	-0.01	2.16	0.31	1.29	-3.64	-2.76	-1.39	-0.89

Model based approach

Imaging Inputs Clinical Data → Analysis engine → Clinically, Biologically relevant information

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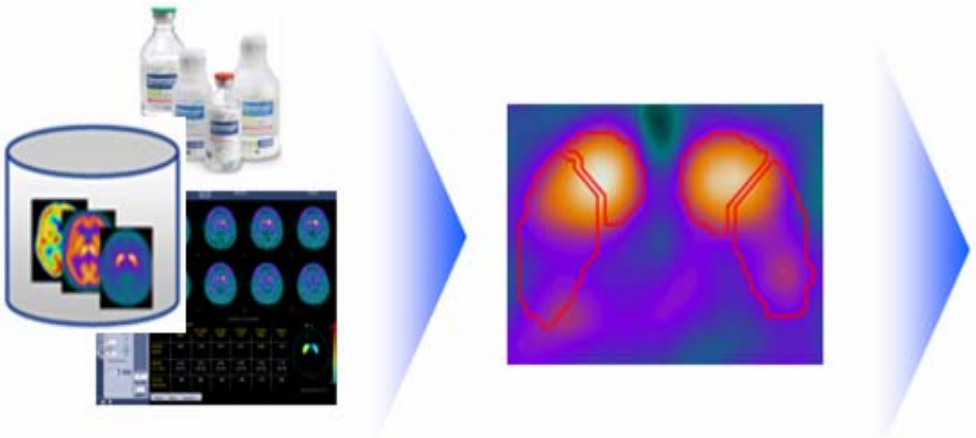
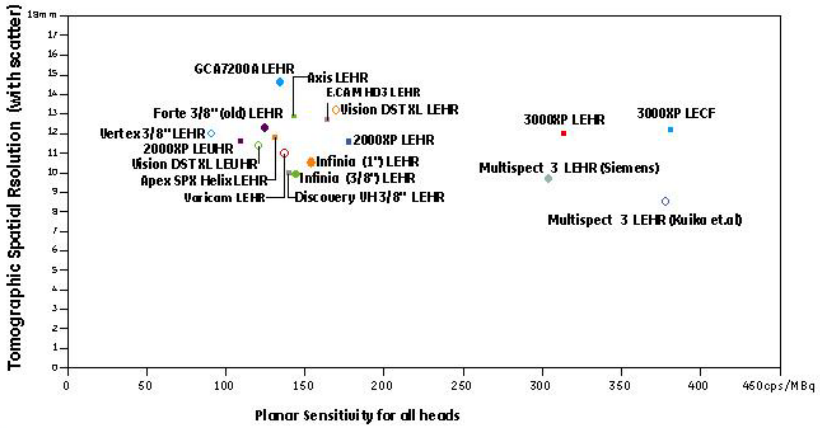
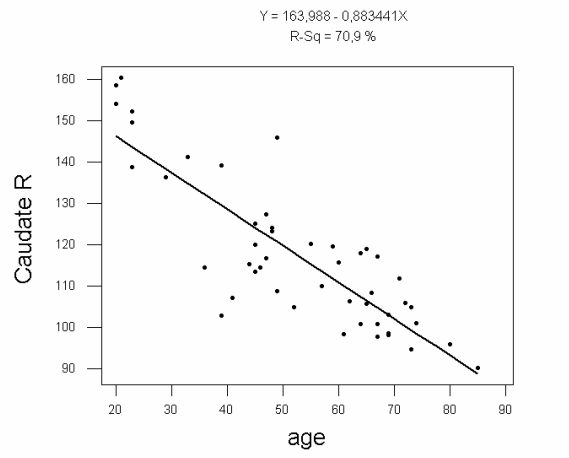
Parkinson's Disease analysis (DaT)



	Striatum Right	Striatum Left	Putamen Right	Putamen Left	Caudate Right	Caudate Left
Patient uptake	0,81	1,01	0,63	0,83	1,01	1,21
Normal (± 1 std)	1,54 (± 0,24)	1,56 (± 0,26)	1,64 (± 0,25)	1,66 (± 0,28)	1,51 (± 0,23)	1,52 (± 0,23)
Percent deviation	- 48%	- 35%	- 62%	- 50%	- 33%	- 21%

$$SBR = Intercept + Slope * Age + C_S * Sensitivity + C_P * PSF$$





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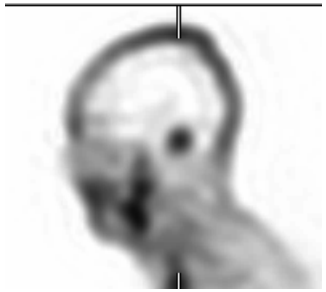
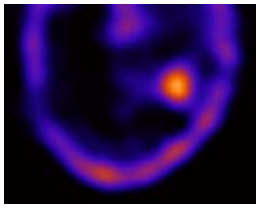
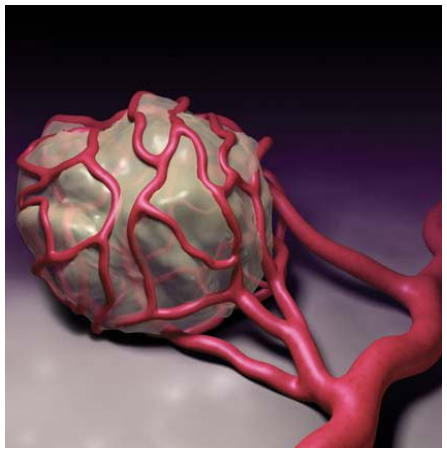
Cancer Therapy monitoring (Angiogenesis)

Pre-therapy: 13 April



Post-therapy: 9 May





It's not just SUVs - Need to understand blood supply to tumor, Perform Attenuation Correction (SPECT/CT or PET/CT)

Build model of tumour biology with inputs from imaging (MR or U/S for flow and perfusion, and SPECT/PET for specific binding to AvB3)

Standardization comes from getting to the "essential" biology of the process. The images are only the start

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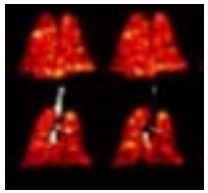
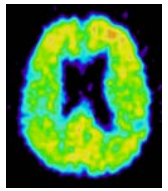
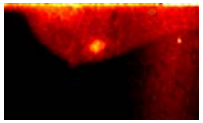
Medical Diagnostics Imaging Network



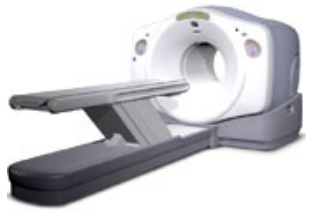




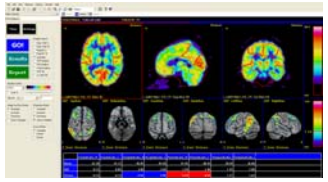
Unique imaging Agents
- XenoSpin
- PIB
- AvB3

Imaging and modelling Phase 1

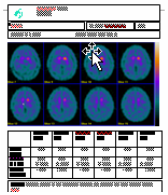
Imaging at IDCs for Phase 2 and 3



Validated, QC-checked networked imaging capability



Unique software tools for analysis



Blinded read infrastructure and data analysis

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Standardization amongst imaging vendors

From commercial perspective – Vendors trying to differentiate themselves
Vendors implement imaging taking account of system imperfections
Standards driven by User demand (e.g. DICOM)
Vendors will not drive this – no User demand or $$

Standards for system performance (QC) would drive quality and "raise all boats"

There is a demand for a common lexicon of imaging and a forum to discuss cross-vendor imaging for Pharma

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